

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
27 November 2003 (27.11.2003)

PCT

(10) International Publication Number
WO 03/098233 A2

(51) International Patent Classification⁷: **G01R**

(74) Agent: **KAVRUKOV, Ivan, S.**; Cooper & Dunham LLP,
1185 Avenue of the Americas, New York, NY 10036 (US).

(21) International Application Number: **PCT/US03/15659**

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(22) International Filing Date: **16 May 2003 (16.05.2003)**

(25) Filing Language: **English**

(26) Publication Language: **English**

(30) Priority Data:
60/381,128 **16 May 2002 (16.05.2002)** **US**

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for all designated States except US*): **ADVANCED MRI TECHNOLOGIES, LLC** [US/US]; 652 Petaluma Avenue, Suite J, Sebastopol, CA 95472 (US).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **GUENTHER, Matthias** [—/US]; 11370 Occidental Road, Sebastopol, CA 95472 (US). **FEINBERG, David, A.** [/US]; 295 Cutlass Court, Bodega Bay, CA 94923 (US). **OSHIO, Koichi** [—/US]; 1716 Apple Creek Lane, Santa Rosa, CA 95401 (US).

Published:

— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **SUSCEPTIBILITY CORRECTION AND CONTRAST ENCODING WITH SIMULTANEOUSLY REFOCUSED MR IMAGES**

(57) Abstract: A method of refocusing multiple images of the same slice position is used to correct for susceptibility errors which cause signal loss in regions of a single EPI image. Each of the simultaneously recorded images is encoded with a different weighting of rephasing by a correction gradient pulse, and these simultaneously recorded images are combined into one image which has signal recovery in the regions of high susceptibility phase errors. This pulse sequence provides simultaneous recording of multiple images on the same slice volume to measure velocity of motion with correction of phase shifts from field inhomogeneity and susceptibility. Additional methods provide different MRI improvements.

BEST AVAILABLE COPY

5

SUSCEPTIBILITY CORRECTION AND CONTRAST ENCODING WITH SIMULTANEOUSLY REFOCUSED MR IMAGES

10 Field

This patent specification is in the field of Magnetic Resonance Imaging (MRI) and more particularly relates to improving imaging by removing or reducing imaging artifacts such as those caused by susceptibility effects and to other
15 improvements in MRI.

Background

Susceptibility artifacts in MRI images are believed to be due to local
20 inhomogeneities in the main magnetic field, and to be caused by local anatomical or physiological features. For example, undesired local magnetic field gradients can occur in the head in regions near air-tissue interfaces near the frontal sinuses and can cause MRI signal loss in the orbital gyrus and in the inferior temporal gyrus and inferior frontal cortex. As
25 pointed out in Yiping Du, Journal Review: Z-Shimming in MRI, 1/14/00, incorporated herein by reference, some of the susceptibility effects may be corrected by post-processing but others are believed to be unrecoverable. Susceptibility artifacts and corrections are discussed in Constable, R.T. and Spenser, D.D., Composite Image Formation in z-Shimmed Functional MR
30 Imaging, Magnetic Resonance in Medicine 42:110-117 (1999), and in

Glover, G.H., 3D z-Shim Method for Reduction of Susceptibility Effects in BOLD MRI, both of which are hereby incorporated by reference.

Despite the progress discussed in the material cited above, and in the material cited in the Journal Review by Yiping Du, it is believed that a
5 need still exists for a more effective reduction or elimination of susceptibility effects.

An echo planar pulse sequence (EPI) is known in MRI and involves using a slice-selective RF excitation pulse applied with a slice-selective gradient to define an MRI signal within a slice volume. The signal is
10 refocused by multiple (n) switchings of the read gradient, during which time n signals are recorded -- one signal refocused after each read gradient switching.

A Burst sequence is also known, where a multitude of hard RF pulses are beamed into the patient during the application of a defocusing
15 gradient. The signals are refocused by a single refocusing gradient, during which time the signals are also phase-encoded for a second axis of spatial resolution. The time of applying plural hard RF pulses, which are not slice selective, is much shorter than the time of gradient switching in EPI, so that the Burst method is faster than EPI. However, the SNR of the Burst method
20 is much lower than of the EPI method, as the signal of the Burst sequence is reduced by fragmentation of the total available signal magnetization proportional to the number of hard RF pulses.

A hybrid of Burst and EPI also has been proposed -- see Heid U.S. Patent No. 6,034,528, incorporated herein by reference. After a Burst
25 sequence, a read gradient is switched in polarity and the echoes in the train created by the hard RF pulses are again refocused. The signals generated by the hybrid sequence are used to generate a 2D FT image by using RF saturation pulses outside of the imaged slice volume. The Burst method uses hard RF pulses that do not have slice selectivity by imposing a
30 frequency modulation on the RF pulse during the application of a slice selective (G_{ss}) gradient with an opposite polarity pulse on the same G_{ss}

axis. The hard RF pulses are applied in much shorter time than the slice selective RF excitations, as required to generate the Burst signals very quickly to avoid T2 decay of signal. The gradient applied during the hard RF pulses of a Burst sequence are on the read gradient axis (G_r) and are used to defocus the magnetization of each RF pulse differently so that they refocus at different times on the switched polarity G_r . Further different from the below described z-shim-SIR sequence, the Burst sequence does not apply gradient pulses between the hard RF pulses, only a single continuous duration of a single G_r gradient that is on at all times during and between the RF pulses. Further different from the z-shim-SIR described below, the Burst sequence combines all of the signals generated by the sequence to make one 2D image, or to make a 3D image by either 2D FT or 3D FT. Also different in making a 2D image, the Burst sequence saturates signals in two regions on either side of a desired image plane; since slice selectivity is not achieved by using the hard RF pulses.

Also known is a Simultaneous Image Refocusing (SIR) pulse sequence, described in co-pending patent application Ser. No. 09/477,783 filed on December 31, 1999 in the name of David Feinberg, a co-inventor in this application, and also described in DA Feinberg, TG Reese, VJ Wedeen, ISMRM 2000, p. 681. The 1999 application and the 2000 publication are hereby incorporated by reference in this patent specification. In the SIR pulse sequence, each of a number of slice volumes is given a respective different phase history. The process then simultaneously refocuses these slice volumes, and acquires the MRI signals from them at respective different times related to their respective different phase histories. For example, two consecutive 90° RF excitation pulses at respective frequencies create magnetization in two slice volumes s_1 and s_2 of a body, such as by using the known MRI practice of employing a main magnetic field and a slice selection gradient field acting on a body. A first dephasing pulse, on a readout axis G_r , is applied after the first but before the second 90° RF pulse, thereby encoding the magnetization of the first slice volume

(s1) but not of slice volume s2 since the second slice volume magnetization has not yet been created. A second dephasing pulse, on the same axis Gr, is applied after both slice volumes have been magnetized by their respective 90° RF pulses and, therefore, encodes the magnetization of both slice volumes equally. This gives the two slice volumes respective different phase histories relative to the Gr direction. If the subsequent readout pulses on the Gr gradient axis are of unit area, and the first and second dephasing pulses on the Gr axis have areas of 0.50 and 0.25, respectively, the magnetization pathways they produce in the two slice volumes will refocus echoes (MRI signals) within opposite halves of each read period, alternating with each EPI (echo planar imaging) gradient switching, due to the respective different phase histories of the two slice volumes relative to the read gradient direction. Thus, in one example an SIR EPI sequence applies two RF excitation pulses on two different slice planes using different frequency offsets with slice-selective gradients. Application of gradient pulses on the read gradient axis, after each RF pulse, causes a different amount of defocusing of the signal created by the two RF pulses. The application of an EPI type of multiple switched read gradients causes refocusing of the two different slice signals to occur at two different times on each switched read gradient. Time reversal of signals further separates the signals from the two different slice planes onto two different areas of the acquired k-space data, which can be digitally separated into two smaller k-space data sets of separated data from each slice. Standard 2D FT (Fourier Transform) gives two slice different image for positions obtained from the single SIR EPI echo train.

While EPI and SIR processes have made significant contributions to MRI, it is still desirable to provide improved MRI processes, and various features of the new processes described below are directed to that end.

30 Summary

One object is to extend correcting for susceptibility signal loss caused by susceptibility defocusing. To this end, a new process creates two or more images from MR signals for the same slice volume, which images have different characteristics, and combines them into a single image that is susceptibility-corrected in a way superior to the known approaches.

In an example of 2D FT EPI images, the new MRI process acquires MRI signals (spins) available in a planar volume during a T2 relaxation period. It modifies the known EPI sequence to refocus signals created from plural RF excitation pulses that are applied with slice-selective gradients.

The multiple magnetizations of spins (m) created by m number of RF pulses are each encoded with a different area of gradient pulse to compensate for a different defocusing effect of the susceptibility-created local gradients that are time invariant and dependent on the object structure and composition. The differently gradient-encoded m magnetizations are then refocused by n EPI read gradient switchings and n phase-encoding gradient pulses to encode 2D FT images. The pulse sequence generates m 2D FT $n \times n$ matrix k-space data sets, with each of the corresponding images having a different gradient encoding to correct for susceptibility defocusing of MRI signals. One of these images has no gradient correction and creates an image that has regions of signal loss due to the susceptibility. The other $m-1$ number of images have MRI signals in the region of susceptibility, according to the refocusing of the defocusing by susceptibility by an equivalent but opposite sign phase shift on spins created by the amplitude-time area of the gradient pulse. As with the known EPI technique, a time reversal is performed on each sequential group of m signals after every other read gradient switching or after alternating read gradient switchings. The m images are created of the same image volume at essentially the same time, essentially simultaneously from the same switched read gradient sequence. Therefore, they experience essentially the same physiologic changes in blood flow and due to any temporally varying physiologic function including

respiratory motions and cardiac pulsations and neurologic stimulations as used for functional MRI studies with BOLD contrast.

The m images are combined using any suitable digital method, and most simply by addition after magnitude display of the data. The combined
5 image created from the addition or other combination of m images differs from a conventional EPI image in that the areas of signal loss caused by susceptibility are filled in with signal recovered in the images using conditioning gradient pulses. The new pulse sequence creates an image
10 with reduced or eliminated areas of signal loss from susceptibility, areas of signal loss that are present in known EPI images. The new pulse sequence thus shows a marked improvement over conventional EPI images by recovering image signal in the regions of the temporal lobes and frontal lobes of the brain, where the susceptibility errors from air in frontal and mastoid air sinuses typically appear.

15 Various aspects and variants of the new process are applicable to sequences other than the known EPI sequence and to achieving results other than suppression of susceptibility artifacts, as discussed in connection with examples described in detail below.

20 Brief Description of the Drawing

Fig. 1 illustrates a known EPI pulse sequence using RF excitation and generating one MRI signal per switched read gradient.

25 Fig. 2 illustrates a known SIR EPI pulse sequence using multiple slice-selective RF pulses, where G_{ss} is applied during each RF pulse that has modulations, and the RF pulses create magnetization on different slice volumes by offsetting the frequency of the RF pulse.

30 Fig. 3 illustrates a new, z-shim-SIR EPI pulse sequence where the same slice volume is irradiated by the slice-selective RF pulses, and conditioning gradient pulses are applied between the RF pulses. The G_c

conditioning gradient pulses can be applied on each gradient axis, Gr, Gp or Gs.

Fig. 4 illustrate a result from using a sequence such as in Fig. 3, where there are two intermediate MR images of the same slice volume but one is affected by the conditioning pulses while the other is not, and the two
5 intermediate images are combined into a single image with reduced or eliminated susceptibility dropout.

Fig. 5 illustrates an example of timing of events in a z-shim-SIR EPI process.

10 Fig. 6 illustrates k-space data collected from the pulse sequence of Fig.3, and a separation of k-space data and the use of FT to create differently conditioned images of the same slice volume.

Fig. 7 illustrates simultaneous acquisition of multiple 2D phase-encoded lines with SIR EPI.

15 Fig. 8 illustrates simultaneous acquisition of multiple 3D phase-encoded partitions with SIR EPI.

Fig. 9 illustrates echo-spacing in k-space.

Fig. 10 illustrates phase-cycled z-shim SIR EPI.

Fig. 11 illustrates a pulse sequence for a 3-image process from two
20 RF pulses.

Fig. 12 shows MR images from the sequence of Fig. 11.

Fig. 13 illustrates a pulse sequence involving velocity encoded pulses.

Fig. 14 illustrates a pulse sequence involving multiple correction
25 pulses.

Detailed Description

Before describing examples of the new, z-shim-SIR EPI and other
30 process, it may be helpful to describe known EPI and the SIR processes to set a background. Referring to Fig. 1, an EPI process involves applying an

RF pulse α° concurrently with a slice-selective gradient pulse on a Gs axis that is followed by a half-width slice selective refocusing gradient of opposite polarity. This is followed in time by readout gradient pulses on a Gr axis that alternate in polarity, starting with a half-width pulse. The half-width pulse
5 on the Gr axis coincides in time with a pre-phasing negative pulse on a Gp axis. Blipped phase-encoding pulses coincide with the start and end of each negative pulse on the Gr axis after the half-width pulse on Gr. The MR echo signals appear after polarity switchings of the Gr pulses, and typically are used to reconstruct and display or otherwise use a conventional MR
10 image.

The SIR EPI process illustrated in Fig. 2 produces MR echo signals for two slice volumes, s1 and s2, in a single echo train. Two 90° RF pulses are applied, F1 and F2. A first slice-selective gradient is applied on the Gs axis at the same time as F1, followed in time by a half-width slice-selective
15 refocusing pulse of opposite polarity on Gs. The second RF pulse, F2, coincides in time with a second slice-selective gradient pulse on Gs, flanked by two half-width slice-selective refocusing pulses of opposite polarity on Gs. Thus, two different slice volumes are defined. A half-width, negative-polarity, conditioning gradient pulse on the Gr axis is halfway between the
20 two RF pulses and the Gs pulses, and a quarter-width, negative-polarity, conditioning gradient pulse is on the Gr axis. The quarter-width pulse on Gr coincides with a pre-phasing pulse on the Gp axis. This gives respective different phase or conditioning histories to the two slice volumes, as the half-width gradient pulse on Gr affects only one of the slice volumes but the
25 quarter-width conditioning pulse affects both slice volumes. Then, full-width read gradient pulses of alternating polarity follow on the Gr axis, and a blipping phase-encoding pulse on the Gp axis matches each polarity transition of the full-width gradient pulses on the Gr axis. Two MR echo signals appear during each of the full-width read gradient pulses, one for
30 each slice volume, thus achieving a number of benefits over conventional

EPI, such as faster acquisition of MR signals for reconstructing two slice images.

One example of the new process is illustrated in Fig. 3 and extends SIR EPI into a z-shim-SIR EPI process by adding conditioning gradient pulses between two RF pulses labeled 60° and 90° : (a) a gradient pulse GsC on the Gs axis; (b) a gradient pulse GrC on the Gr axis; and (c) a gradient pulse GpC on the Gp axis. Unlike the SIR example earlier discussed, the two slice-selective gradient pulses that coincide in time with the two RF pulses, Gs1 and Gs2, select the same slice. Also unlike the SIR example, there are two pre-phasing gradient pulses on the Gp axis, a positive pulse GpP1 that coincides in time with the negative-polarity half-width pulse GsP2 on the Gs axis, and a negative-polarity GpP2 pulse that follows in time the quarter-width pulse GrP2 on the Gr axis. The other gradient pulses on the Gr and Gp axis match those in the SIR example. In particular, Gs1 is a slice-selective pulse for the slice volume, as is Gs2. GsR1 and GsR2 are slice-selective refocusing gradients. GrP1 is a pre-phasing pulse for Gr to shift the position of signals s1. GrP2 is a pre-phasing pulse affecting the positions of signals s1 and s2 on the readout period. Gr+ and Gr- are positive and negative polarity readout gradient pulses. GpP1 and GpP2 are pre-phasing gradient pulses on the phase-encoding axis, and GpBlip are blipped phase-encoding gradient pulses.

In Fig. 3, two sets of MR echo signals are obtained, a set labeled s1 and a set labeled S2. Unlike the SIR example, here the two sets are for the same slice volume. However, they contain different information about that slice volume. The conditioning gradient pulses affect one of the two sets of MR signals but not the other. Thus, two MR images can be reconstructed for the same slice volume, using for example conventional FT processing for each. One image is from the set of MR signals affected by the conditioning pulses and one from the set that is not so affected. Stated differently, one of the MR images is corrected, but the other one is not. When the two MR images of the same slice volume are combined, by adding them or using a

more sophisticated combination of the two, the resulting combined MR image is superior – for example it suppresses susceptibility dropout.

Fig. 4 illustrates an example of such MR signal acquisition and the resulting two initial MR images that are for the same slice volume (but contain different information), and the MR image resulting from combining the two images, in this case by simple addition. The left image is the image that is not affected by the conditioning gradient pulses; the center image is the one affected by those pulses, and the right image is the result of combining the left and center images and demonstrates a reduction or elimination of susceptibility dependent signal dropout.

Fig. 5 illustrates timing of events in the process of Fig. 3. The EPI sequence is modified by applying at least one additional RF excitation pulse prior to the switched gradient readout of signals. Each RF excitation pulse creates signal from the same slice volume. A conditioning gradient is applied on the read gradient axis during the period between the RF excitations to encode a different signal defocusing on signals from each respective RF excitation. The amount of signal defocusing is determined by the polarity and gradient pulse area (A), and the amplitude–time relationship ($\gamma \cdot G_r \cdot T_p$) where γ is the gyromagnetic constant, G_r is the amplitude of the gradient pulses applied on the gradient read axis (milliTesla/meter) and T_p is the duration (millisecond) of the gradient pulse. After the time of the RF pulses and the defocusing gradient pulses, a multitude of switched readout gradients are applied to create multiple additional signal refocusing as in an EPI echo train sequence. The switched readout gradients refocus the signal from the RF pulses at different times during the readout gradient. The time of each signal refocusing is determined by the net sum of the defocusing gradient experienced by the signal. The MR signal created by the first RF excitation pulse experiences the net sum of all defocusing gradient pulses applied after the first RF excitation pulse. The MR signal created by the second RF excitation pulse does not experience the defocusing gradient pulses applied prior to the second RF excitation pulse.

Therefore the first and second MR signals differ in defocusing by the conditioning gradient pulse applied between the respective first and second RF excitation pulse. This difference in defocusing of the MR signals causes the signals to be refocused at different times or locations on the read
5 gradient pulse. The MR signal is refocused at a time when the time integral of the readout gradient creates a phase refocusing equal to the net defocusing of the signal. After each read gradient period, there is a switching of the polarity of the read gradient, similar to known EPI sequences, which continues the process of refocusing additional signals on
10 each subsequent read gradient. The timing of the first and second signals is reversed in each switched read period. At the end of the EPI echo train sequence, the signal from each RF excitation is interleaved into every other signal of the collected data. After time reversal of the signals from every other read period, the two sets of signals from different RF excitations are
15 on opposite sides of k-space on the k_r axis.

As illustrated in Fig. 6, the k-spaces of two separate images are obtained by dividing the data matrix around the center of the k_r -axis. The resulting two k-space sets of signals are simultaneously phase encoded in the echo train by gradient pulses (G_p) for a second axis of resolution either
20 using a blipped or continuous G_p gradient waveform during the echo train. Standard 2D Fourier Transform (FT) of each of the k-space data sets is made to produce the two images at the identical slice position, or some other suitable image reconstruction method can be used.

Now that it is explained how two different images of the same slice
25 volume are created from two different RF excitations using one sequence of multiple switched G_r gradients, as in an EPI sequence, it can be further understood how these two images can be encoded separately to correct for susceptibility. Any suitable type of gradient or RF pulse used for a susceptibility correction scheme that is applied after the first RF pulse will
30 encode the signals of the first RF pulse. However, just as the signal created by the second RF excitation pulse does not experience the defocusing

caused by Gr2 gradient pulses applied prior to the second RF excitation pulse, the second signal does not experience the correction or conditioning scheme pulses. Similarly, a net sum of correction or conditioning scheme pulses is experienced by the signal beginning at a time in the sequence
 5 when the respective RF excitation pulse creates the signal, not including sequence time prior to the RF pulse. The term "phase history" is introduced to define this net accumulated defocusing of the gradient pulses applied during the time of the signal, which excludes pulse sequence effects prior to the RF excitation pulses that create the signal.

10 Susceptibility correction schemes involve the application of gradient pulses to compensate or refocus the linear components of the local gradients (G_L) created by susceptibility. Signal loss is caused by susceptibility. This effect is due to local magnetic field gradients in the head in regions near air – tissue interfaces. These regions occur near the frontal
 15 sinuses and cause signal loss in the orbital gyrus, and the inferior temporal gyrus and inferior frontal cortex. The defocusing caused by the local gradients of susceptibility is independent of other gradient pulses applied during the pulse sequences, however the net defocusing due to susceptibility is largely determined by the TE of the sequence, the $T2^*$, as
 20 $(G_L \cdot TE) = D^*$ where the defocusing of the signal (D^*) is the contribution made by linear components of the local gradients of susceptibility. D^* is refocused (R^*) by the combined effect of specific compensation gradient pulses (G_c) of duration T_c , where $R^* = G_c \cdot T_c$, such that there is refocusing of the signal loss by D^* by the relationship $(D^* + R^* = 0)$. In the same
 25 image that has this susceptibility correction by G_c gradient pulse, the signal in other regions of the slice that do not have local susceptibility effects is defocused by G_c . These regions therefore experience a loss of signal. Therefore, the new process creates at least two images, one which has G_c and R^* correction of susceptibility and a second image that does not have
 30 R^* correction. A combination of the two images creates a net image in which there is recovery of signal in regions where the defocusing effect of

local susceptibility gradient is nulled or refocused by the applied G_c gradient pulse. The net effective G_c gradient pulse is applied between the two RF excitation pulses, so in effect the image created by the first RF excitation pulse has the recovery of signal in regions of susceptibility local gradients.

5 The image derived from the second RF pulse does not experience the G_c pulse, and therefore it has a signal loss in regions of susceptibility but normal signal in all regions of the slice where there is no susceptibility effect. In a single shot echo train, these two images are acquired. These two images are combined to create a final image that has signal recovery in
10 regions of high susceptibility where the rephrasing of G_c pulse equals the defocusing of the local susceptibility gradients. At regions where D^* does not equal R^* , there is signal loss. Nevertheless, by appropriate adjustment of G_c , much of the signal loss in EPI images is recovered in the corrected image from the combination of two simultaneously acquired data sets.

15 A variant of the above pulse sequence is to encode 3 (or more) images in each sequence. The method can then be extended so that two (or more) images with different R^* values are encoded and one image has no R^* . One method of creating 3 different signals is by using 3 RF excitation pulses. Another way to create a third image is to create a spin echo signal
20 by refocusing the signal with two RF pulses. Some of the signal created from the first RF pulse is refocused by the second RF pulse to create a second set of signals with a different phase than the remaining signals created by the first RF pulse. This can be extended to more than three images.

25 A different variant of the above described method and technique is to correct for susceptibility and main magnetic field inhomogeneity errors in MR images that show velocity of motion of spins. An example of a suitable pulse sequence is illustrated in Fig. 13. The multiple images of the same slice volume are encoded with different velocity-dependent phase encoding
30 pulses. By combining (e.g. adding) the velocity phase images, measures of velocity can be obtained while the signal phase changes caused by

susceptibility and field inhomogeneity are reduced or removed from the velocity image. By applying a bipolar gradient pulses, G_v , as taught in paper by Moran in J. Magnetic Resonance Imaging, 1982, a signal phase is proportional to velocity of spins moving along the applied gradient axis.

- 5 This pulses G_v are labeled G_{sv} in Fig. 13. The phase of the signal is also determined by the linear added effect of time spent in a local susceptibility gradient and in the inhomogeneity of the main magnetic field, together called phase errors, E_p . The E_p can be nulled by encoding the two images with equal but opposite velocity phase shift and combining the two images
- 10 so that the velocity phases are coherently combined while the E_p are nulled. One approach is to apply a G_v pulse between the first and second RF excitations and a second G_v pulse after the second RF excitation where the first G_v pulse has twice the gradient amplitude and opposite polarity, $-2G_v$. The image from the first RF excitation has a net phase of $(G_v - 2G_v)$ equal
- 15 to $-G_v$. The image created by the second RF excitation does not experience the first $-2G_v$ pulse and has a net phase contribution by only the second gradient pulse, $+G_v$. The net phase shifts in the images also include the effects of E_p . A linear complex combination of the data from the two acquired images nulls the E_p contribution to phase and leaves a combined
- 20 image with only velocity dependent phase (P_v), where $(\text{Image1} (-P_v + E_p) - \text{Image2} (+P_v + E_p) = \text{Image3} (P_v))$. A final image has velocity phase (P_v) which is corrected for E_p and is dependent on G_v and the duration of G_v . Many different combinations of G_v pulses on G_x , G_y and G_z axis can be applied, so that several final E_p corrected images are obtained. In fact, the
- 25 velocity vector components V_x , V_y , and V_z can be obtained from the same echo train sequence, all of which are corrected for E_p . This would require as many as 6 RF excitation pulses to create 6 images with different values of P_v dependent on G_v applied on three different gradient axis. An appropriate linear combination of the acquired images gives a phase image
- 30 obtained from the complex data to display P_v as a measure of velocity.

Other encoding methods can be applied as gradient pulses between the RF excitation pulses. One example is illustrated in Fig. 14.

Combinations of either Gc or Gv applied between RF pulses gives corresponding images of a spatial region obtained simultaneously from a single echo train. Also, the sequence can be repeated in iterative cycles (c) during different TR periods with varying either the Gp phase encoding pulse areas, or with different Gc or Gv pulses. The additional cycles of the sequence can be combined to make higher spatial resolution. Yet a different useful variant is for the additional c cycles of the sequence to be used to make additional images of the same slice region, each image using a different Gc or Gv so that additional correction images are obtained and used to be combined into the final image for improved correction of susceptibility or measurement of velocity.

Conditioning gradient pulses can be used for purposes other than, or in addition to, reducing or eliminating susceptibility dropout. Fig. 7 illustrates an example that is otherwise similar to Fig. 3 but omits the conditioning gradient pulses of Fig. 3 and applies different phase-encoding to the same slice volume by means of a conditioning gradient pulse GpBlip applied on the Gp axis, in the time between the two RF pulses. An advantage of this variant compared to a conventional EPI pulse sequence lies in the time saving. If a conventional EPI sequence uses N phase-encoding lines (e.g. N=128), then it has to switch the gradients at least N-1 times. The variant illustrated in Fig. 7, which uses two excitations, each differently phase-encoded, reduces the number of gradient switchings by more than a factor of 2, to be precise, to N/2-1.

Fig. 8 illustrates a similar approach but applied to 3D phase-encoding partitions. Here the gradient G3dP1 is placed on the slice-select axis Gs, between the two RF pulses, and an opposite polarity gradient G3dP2 is on the same Gs axis, but follows the second RF pulse. The sequence variant for 3D-encoding makes it possible to acquire two (or more) different 3D

phase-encoding steps within one echo train, thus yielding a shorter measurement time.

In the examples of the new process discussed above, the echo sampling is symmetric, i.e. if the acquired k-space data is cut in half, the echoes are falling into the middle of each part. However, it is possible to use an asymmetric readout, which allows separating the echoes within the k-space (moving them further apart). This reduces the interference of the high frequency components of the echoes and can be used to minimize image artifacts. To achieve this separation the pre-phasing gradients in the read direction can be changed.

Therefore, an asymmetry-factor k is introduced, which is 0 for symmetric readout and 1 for completely asymmetric readout, where the echo lies at the edge of acquired k-space. Then, the total momentum of Gr1P and Gr2P is calculated as follows:

$$\text{totalMomentum(Gr1P)} = \text{totalMomentum(Greadout)} * 1/2 * (1+k)$$

$$\text{totalMomentum(Gr2P)} = \text{totalMomentum(Greadout)} * 1/4 * (1-k).$$

Fig. 9 illustrates echo spacing for three k-values, and shows that echoes are centered in k-space at $k=0$ but move further apart from each other as the value of k increases.

As illustrated in Fig. 10, phase-cycling can be used to separate the signals of the RF pulses. This allows the echoes of all RF pulses to fall on top of each other. This corresponds to an asymmetry-factor $k=-1$. But, multiple acquisitions are performed to phase-cycle the RF pulses, which places limits on the advantage of the method to acquire multiple images with different conditioning at the same time. The information can be acquired at the same time but averaged over the multiple acquisitions. In standard imaging techniques the information is not averaged over time, because separate readout periods are used, and the signals are acquired to different time points, which can yield significant artifacts due to motion, physiological changes, etc. To increase time efficiency, the different phase cycles can be encoded within one echo train, by using both phase-cycling and SIR-technology. As shown in Fig. 10, two RF pulses α_1 and α_2 are applied, which have different zshim-values, according to the gradient

pulse GsC between them. The difference here is, that no read gradient is applied between $\alpha 1$ and $\alpha 2$, thus making the echoes fall on top of each other and forming the signal s12. After those two RF pulses $\alpha 1$ and $\alpha 2$, a defocusing gradient pulse separates the combined signals s12 from the next two signals s34, which result from the RF pulses $\alpha 3$ and $\alpha 4$. The phase of $\alpha 4$ is changed by 180° compared to $\alpha 2$. This allows the process to separate the signals s1 and s3 from the signals s2 and s4 by simply adding or subtracting the divided k-space data, respectively. Thus in turn allows the process to suppress signal leakage from one MR image to another image that has different conditioning. Differences in the phase evolution due to the slightly different echo times can be addressed by adding an additional pre-phasing gradient pulse GpP, which moves the echo of the RF pulses $\alpha 1$ and $\alpha 2$ to an earlier line in k-space than the echo of $\alpha 3$ and $\alpha 4$. For this, the distance between $\alpha 1$ and $\alpha 3$ (the same as the distance between $\alpha 2$ and $\alpha 4$) is a multiple of the time needed to acquire a single line in EPI readout. This factor gives the number of phase-encoding lines the echoes of $\alpha 1$ and 2 have to be shifted up. This method shows some similarity with POMP, where two different slices are acquired together and are separated by phase-cycling, too. However, unlike POMP, in this variant of the new process the summed signals originate from the same slice volume.

The new process is not limited to the type and number of conditioning gradient pulses used in the examples discussed above. For example, instead of using only one conditioning gradient pulse Gc1, which is located between the two excitation pulses RF1 and RF2, it is possible to add another conditioning gradient pulse Gc2 after RF2. In general, the magnetization that is excited by RF1 "feels" the sum of both conditioning gradients Gc1 and Gc2, while the magnetization that is excited by RF2 only "feels" the effect of Gc2.

In some of the above examples two excitation pulses RF1 and RF2 are used to produce two independent images with different conditioning. However, the new process is not limited to only two simultaneously refocused images. One way is to add more RF excitation pulses to produce more primary echoes, which can be encoded according to the described method for two excitation pulses

(addition of pre-phasing gradient pulse along the read-direction, called Gr1P above). However, the signal-to-noise ratio is likely to be reduced since more RF pulses are applied on the same slice volume. An ISMRM abstract that the named invention have prepared for publication, but which is not published as of the filing date of this patent application, describes how three images can be encoded with only two excitation pulses RF1 and RF2. The second RF pulse RF2 will not only produce a primary echo, but also act as a refocusing SE-echo pulse on the magnetization of the first RF pulse RF1. This will yield a spin echo after RF2, which can be used for image acquisition, too. Therefore, not only two but three images can be acquired, which have different conditioning, such as different z-shim correction values. However, the amount of conditioning of the three images is not independent any more. Since the magnetization, which forms the spin echo, was reversed by RF2, the phase history of those spins is mirrored. i.e. using two conditioning gradient pulses Gc1 and Gc2 after application of RF1 and RF2, respectively, the primary echo of RF1 experiences the effect of Gc1+Gc2, while the primary echo of RF2 is prepared with Gc2 only. However, the spin echo of RF1, which is produced by RF2, "feels" -Gc1+Gc2. If the values of Gc1 and Gc2 are adjusted appropriately, three differently conditioned images can be acquired with two RF excitation pulses. The inventioned can be extended to use multiple RF excitation pulses, more than two pulses, to create pleural signals. The invention can be combined with additional pre conditioning RF pulses and gradient pulses which eliminate lipid signal and leave only water signal in the image.

A novel EPI sequence described in the ISMRM abstract that is yet unpublished is used to eliminate susceptibility dependent signal drop out in the brain, limiting to fMRI. The process simultaneously acquires 3 different gradient compensated images at the identical slice plane or volume and essentially at the same time. The net combined single shot T2* S/R EPI image recovers the signal lost due to susceptibility in the temporal and frontal lobes of the brain.

Echo planar imaging is extensively used for functional MRI and brain activation mapping. EPI has well characterized susceptibility artifacts causing

signal drop out in brain regions adjacent to air tissue interfaces in the inferior temporal lobes, gyrus rectus and orbitofrontal lobes. This problem of incomplete brain coverage is perhaps the major imaging problem remaining in brain activation studies. Several methods have been developed to recover

5 susceptibility signal loss by means of applying magnetic gradients to correct for local field inhomogeneity. These methods require repeating the EPI sequence with multiple excitations with different gradient correction pulses, or z-shim. This lengthens the imaging experiment and imposes further constraints in performing single trial studies. A novel EPI sequence incorporates the Simultaneous Image

10 Refocusing (SIR) technique to overcome susceptibility artifacts in single shot EPI while maintaining T2* weighting for BOLD contrast. The earlier described SIR technique acquires multi-slice images in a single echo train using multiple excitation RF pulses, simultaneously refocusing all signals with each polarity switching of the read gradient. It is modified to simultaneously obtain multiple

15 images of the same slice volume in one echo train. The simultaneously acquired images are encoded with different gradient correction pulses and combined to form a single shot EPI image with recovery of the susceptibility signal drop out in the brain.

Fig. 11 illustrates this sequence. Two slice selective RF pulses are applied

20 to the same slice location. Three signal components are generated as the result, namely 2 FIDs, one from each RF pulse and an echo generated by the two RF pulse. These signals share the same phase encoding, but are separated along the readout direction. Each signal component receives a different net area of the gradient pulses for susceptibility correction, applied on the slice direction (Gs).

25 With a single shot data acquisition, three complete images are obtained. These images are combined after normal 2D FT image reconstruction to make an image without signal dropouts.

The sequence was implemented on a Siemens 1.5T Sonata scanner. Typical imaging parameters were: single shot, T2* TE = 50 msec, 256 x 64

30 matrix, which is separated into three 85 x 64 images, FOV = 30 cm, slice thickness = 5 mm. Fig. 12 shows in-vivo images of a healthy volunteer chosen

from a multi-slice acquisition in regions of most severe signal drop-out. The top row shows images reconstructed using only signals from FID 1, which does not receive any correction gradient, essentially a conventional T2* EPI. The Lower row shows the SIR EPI images using all three components combined, including FID 1. In comparing the signal drop out regions, it is critical to note that the EPI (top row) and SIR EPI (lower row) have identical T2* weighting at TE of 50msec.

The multi-slice SIR EPI sequence successfully reduces or eliminates susceptibility dependent signal drop out in the brain's orbito-frontal cortex and temporal lobes, which limits conventional EPI sequences with the same T2* weighting. SIR EPI, therefore, provides greater image coverage of the brain as needed for many fMRI experiments. It is significant that the signal drop out regions are recovered in a single shot sequence, unencumbered by longer acquisition times from sequence repetitions needed by other susceptibility correction schemes. The new single shot SIR EPI sequence provides intrinsic gradient correction and recovery of signal in brain regions of high susceptibility, limiting EPI sequences. SIR EPI therefore may likely provide significant improvements over conventional EPI in functional MRI experiments.

Hard (non-selective) RF pulses can be used to reduce the time spent for excitation and thus reduce the time distance (and phase evolution) between RF pulses. This is similar to BURST-like techniques, where multiple hard RF pulses are used with different phase encoding steps to form an image. In contrast, the new process can use the hard RF pulses not to form one image but to form multiple images with different conditioning, which is performed between (and after) the RF excitation pulses. To achieve slice selectivity, saturation pulses can be applied, to suppress all but the wanted slice, in a manner similar to that proposed in the Heid patent incorporated by reference herein.

Persons skilled in this technology will understand that the above examples are not limiting to the scope of the disclosed process, and that many variations are possible within the teachings set forth above, and that MRI systems configured to carry out the disclosed processes, such as by suitable pulse

sequence or software changes, constitute new machines that are within the scope of the disclosure herein.

5

10

15

20

25

30

What is claimed:

1. An MRI method comprising:
 - 5 subjecting a body to a main magnetic field;
 applying to the body a first RF excitation pulse and a first magnetic field gradient to define a volume in the body, and later applying to the body a second RF excitation pulse and a second magnetic field gradient to define the same volume;
 - 10 giving the volume defined by the first RF pulse and first gradient a phase history different from that of the same volume defined by the second RF pulse and second gradient
 obtaining first MRI signals for the volume as excited by the first RF pulse, and second MRI signals for the same volume as excited by the second RF pulse;
 - 15 said first and second MRI signals alternating in time;
 reconstructing a first MRI image from the first MRI signals, and a second MRI image for the same slice from the second MRI signals;
 combining said first and second MRI images into a net image; and
 using said net image.
- 20 2. An MRI method as in claim 1, in which said different phase histories are selected to give one of the first and second images a correction of susceptibility different from any such correction of the other image.
- 25 3. A method as in claim 1 in which said gradients are slice selecting gradients
4. An MRI method comprising:
 - 30 obtaining substantially simultaneously MRI signals for two images of the same volume encoded with a different weighting or rephasing by correction magnetic gradient pulses;

combining information derived from said MRI signals into an image that has signal recovery in regions of high susceptibility phase errors.

5

10

15

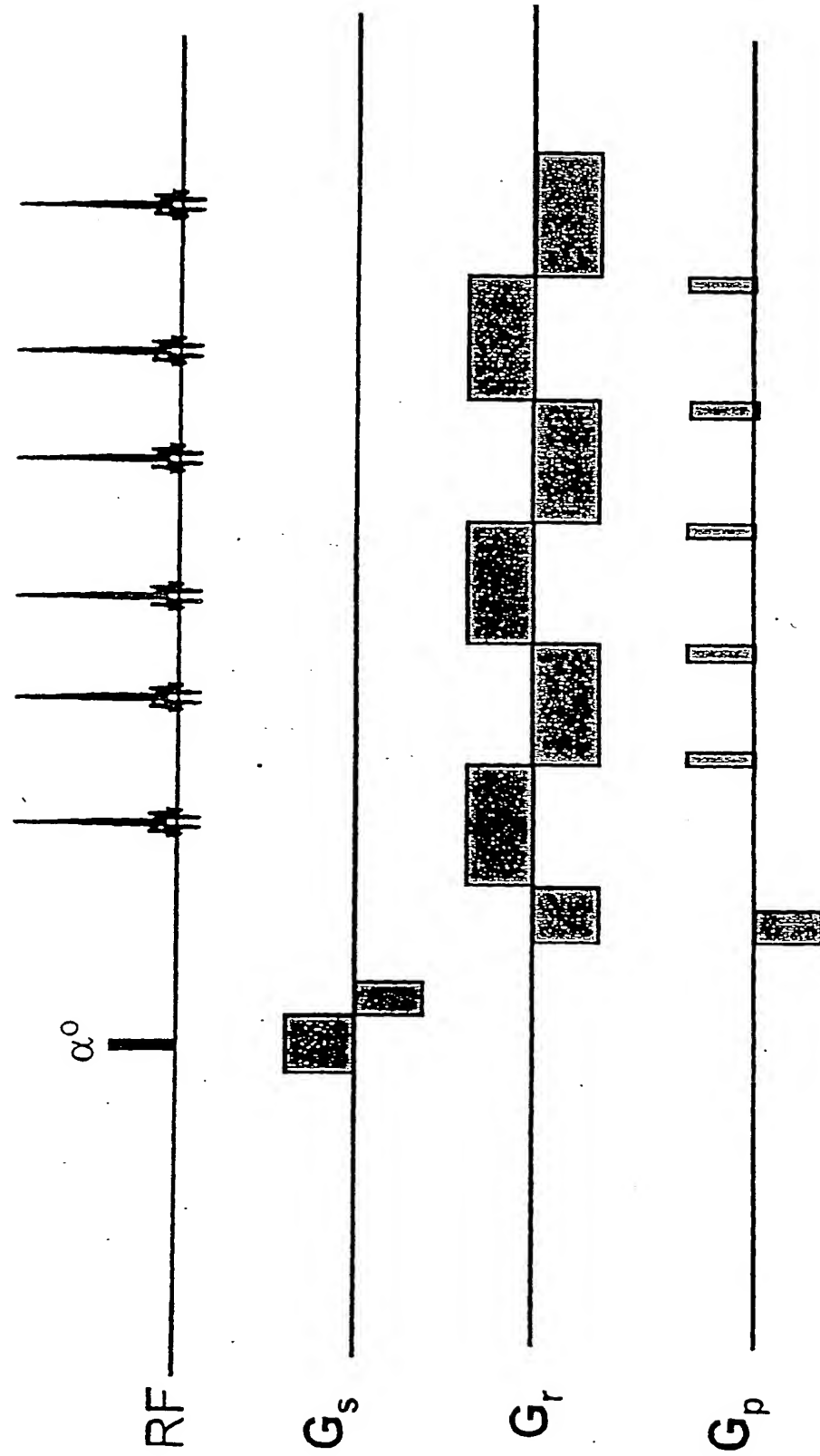
20

25

30

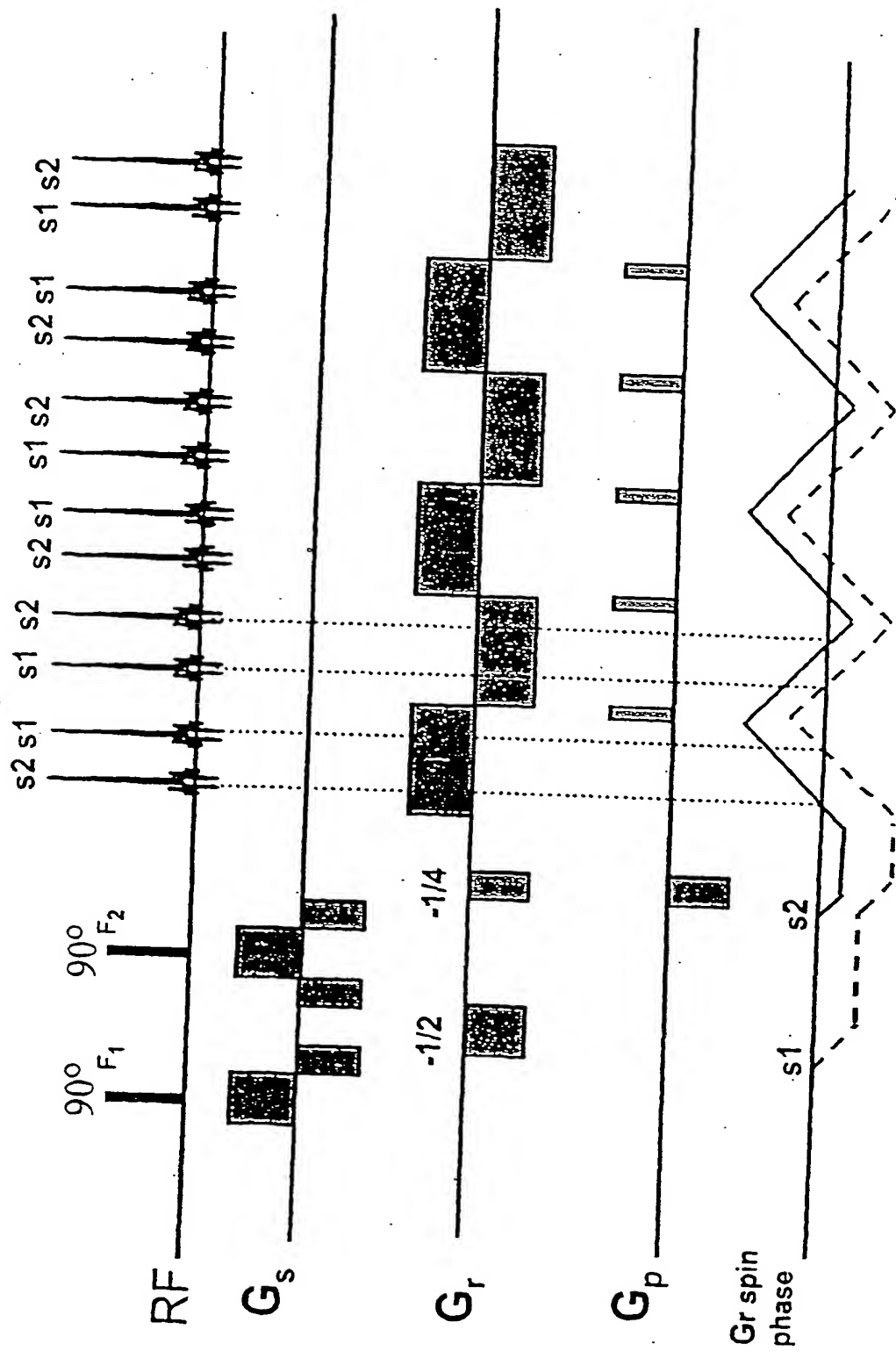
EPI

FIG. 1



SIR EPI

FIG. 2



z-shim-SIR EPI **FIG. 3**

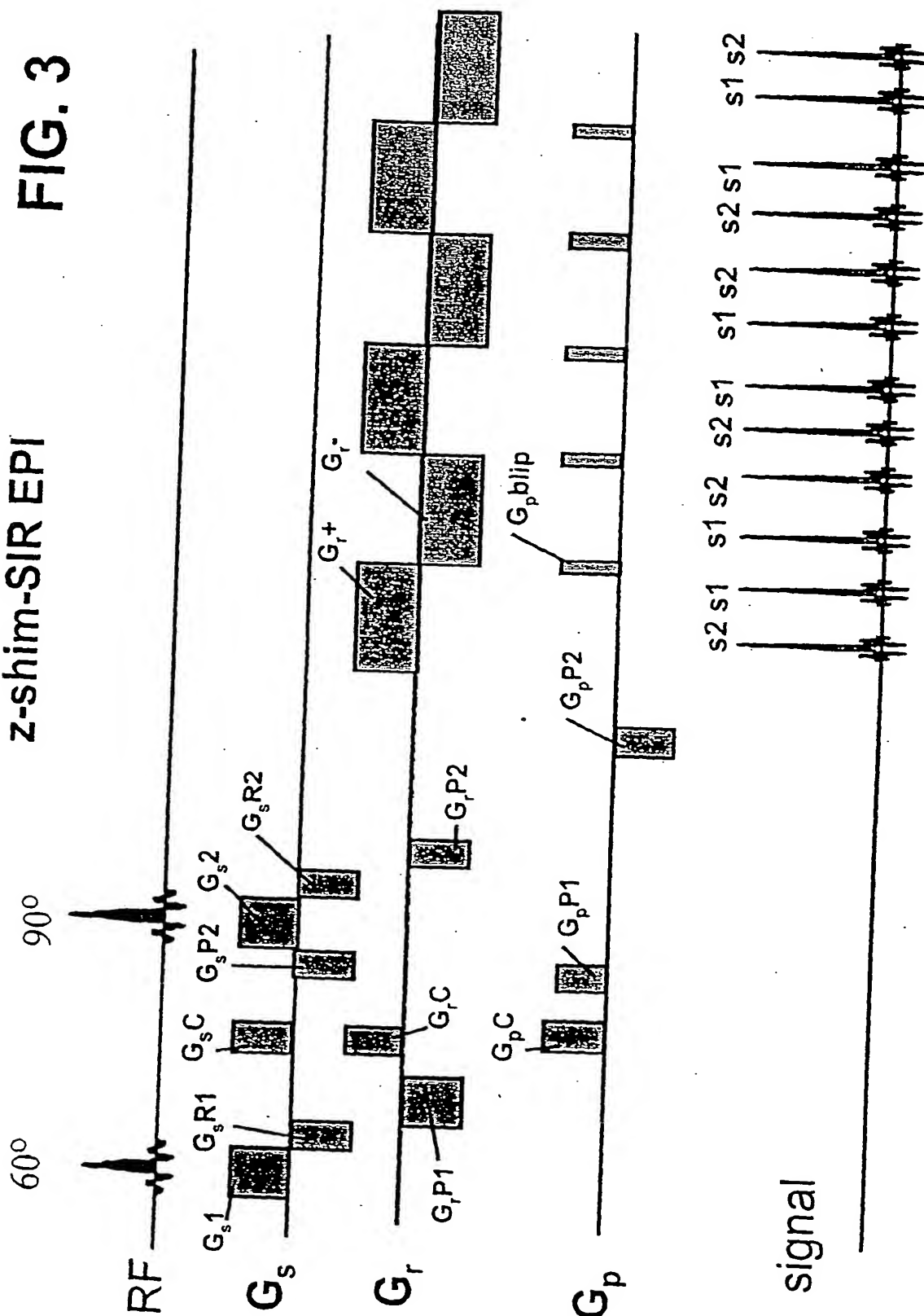
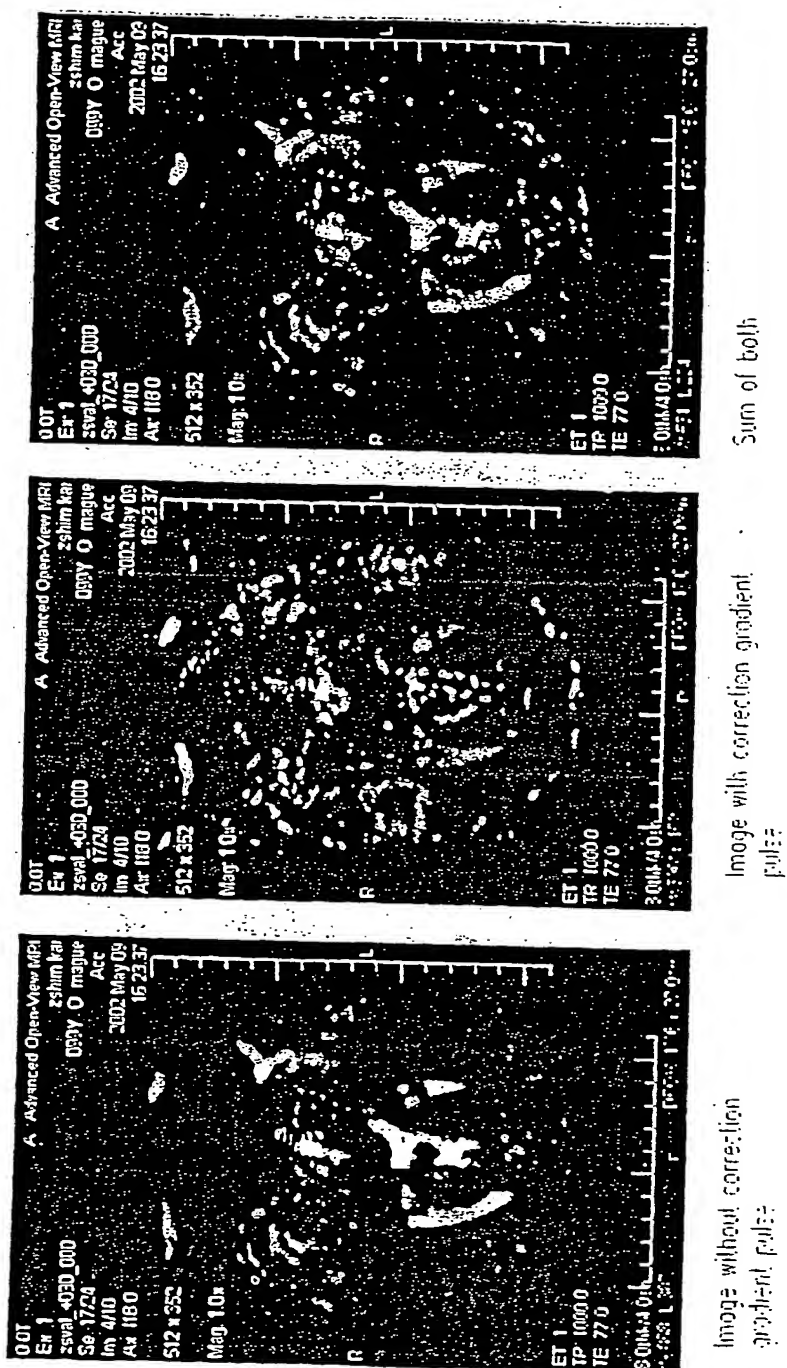
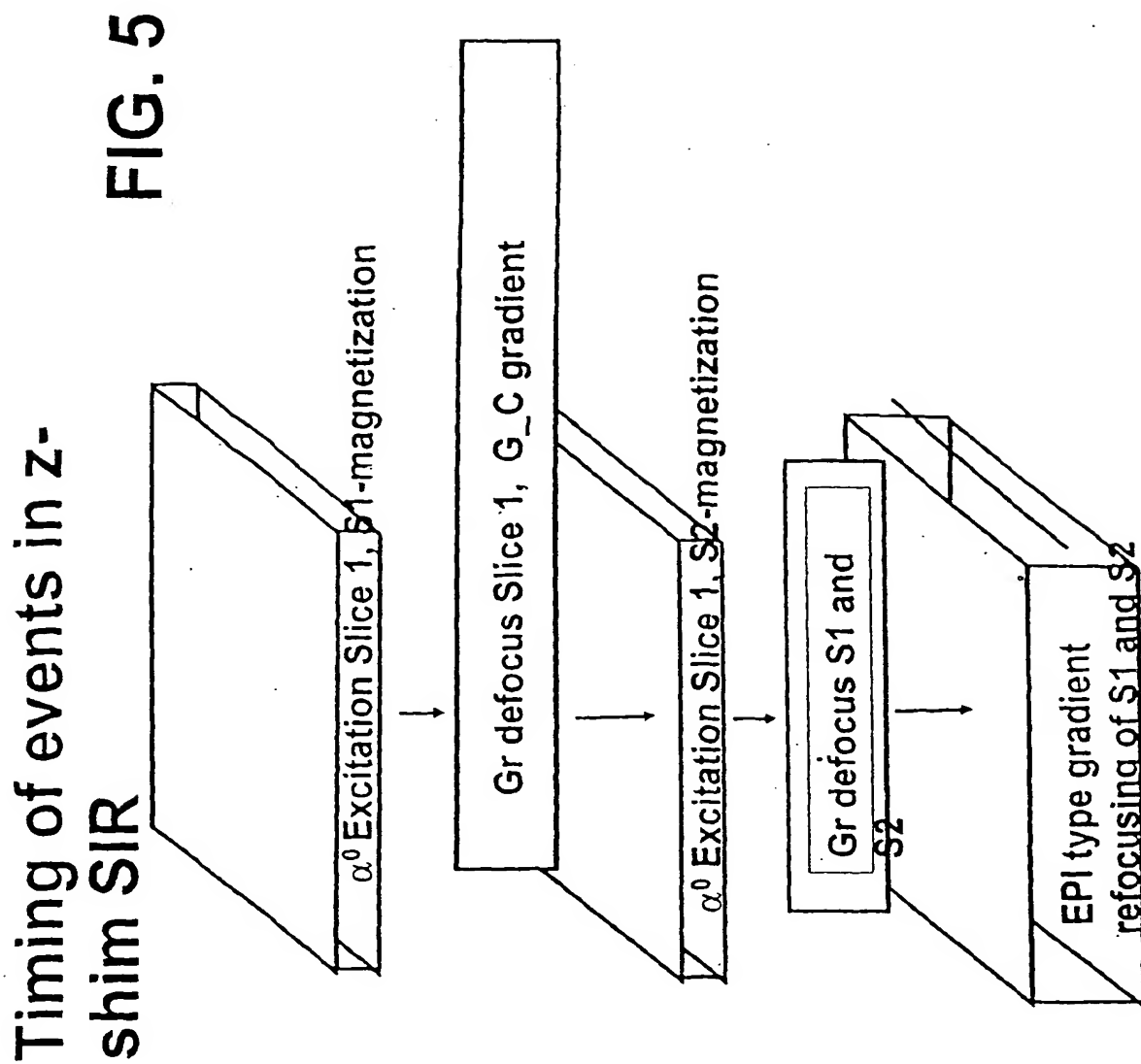


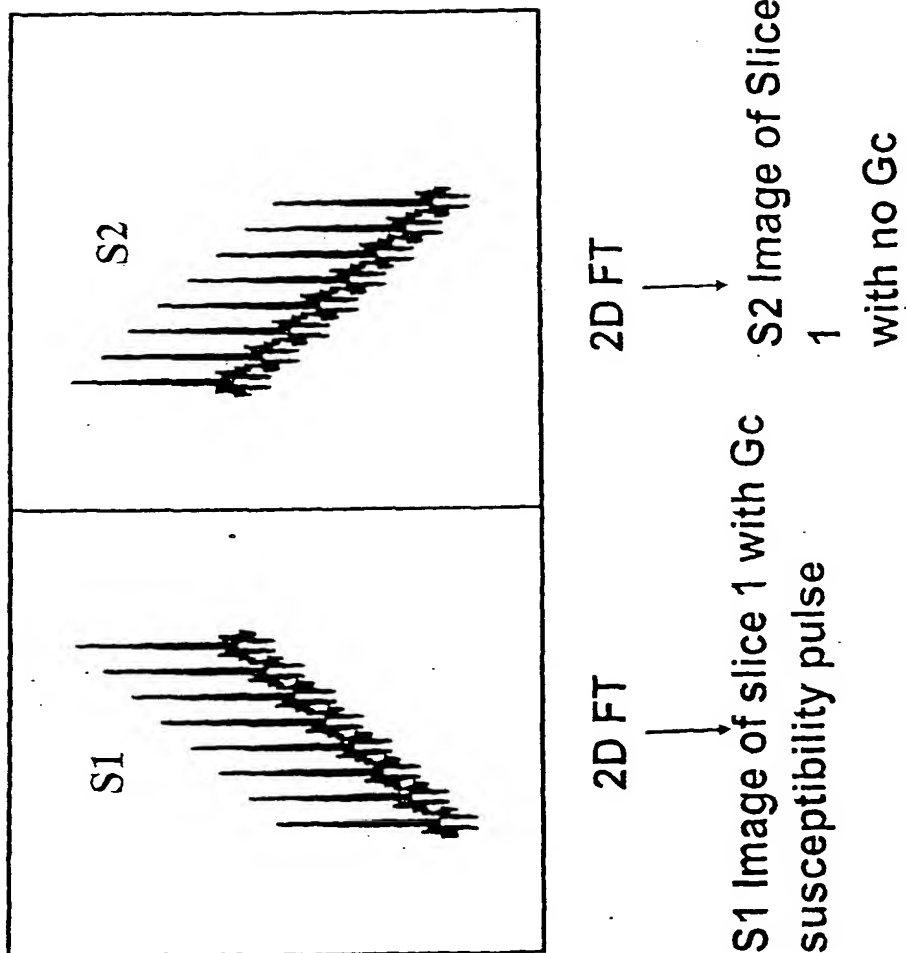
FIG. 4





k-space data collected

FIG. 6



simultaneous acquisition of multiple phase-encoding lines with SIR EPI

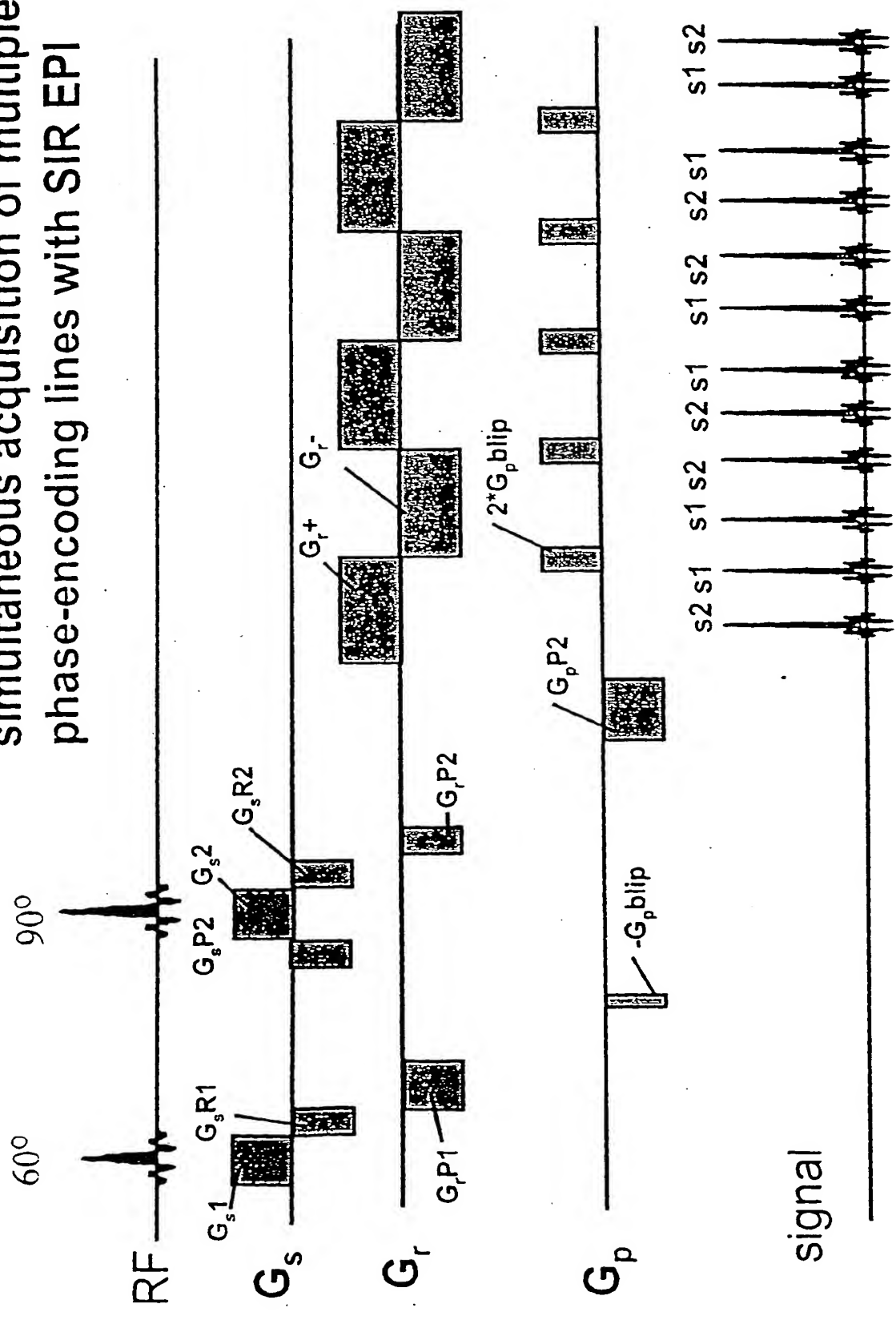
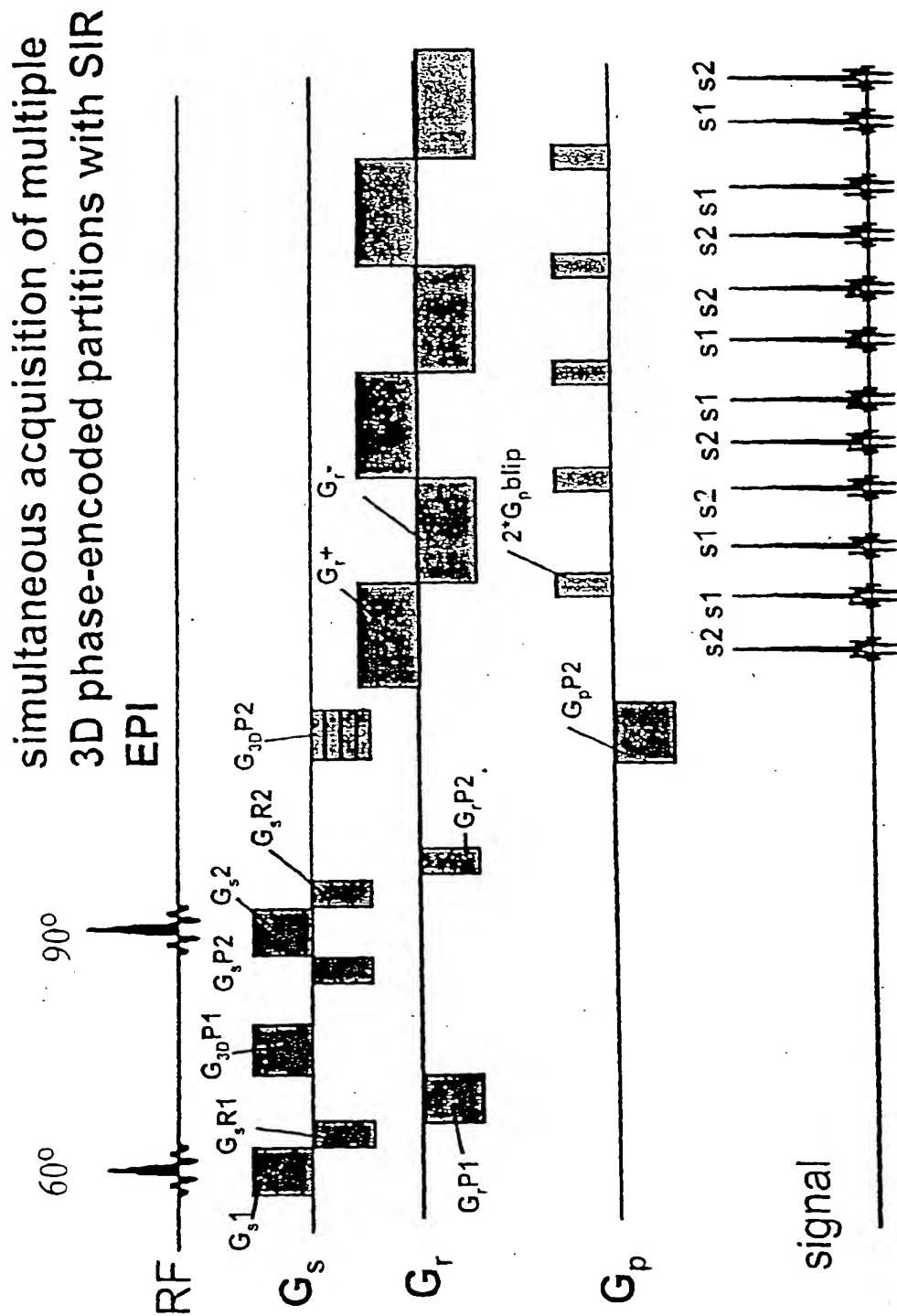


FIG. 7

FIG. 8



Echo spacing:
Moving echoes further apart in k-space

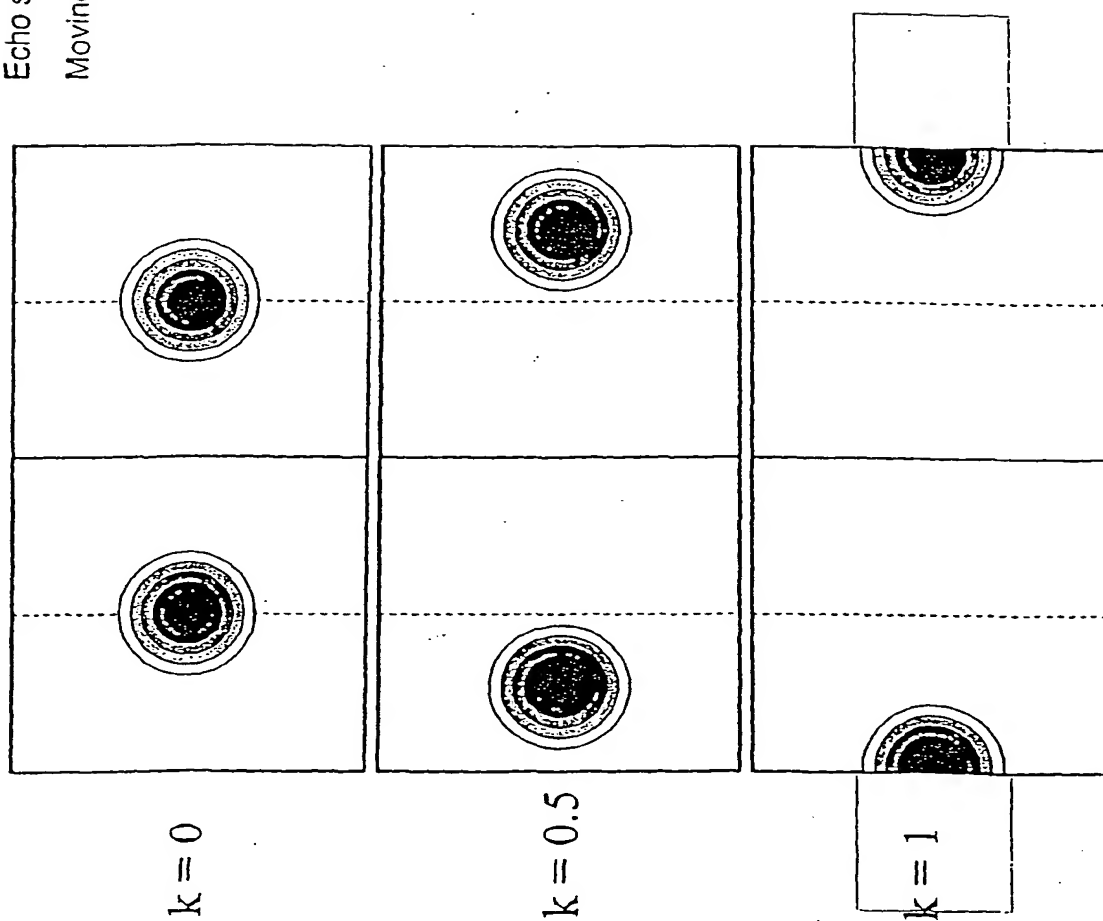


FIG. 9

FIG. 11

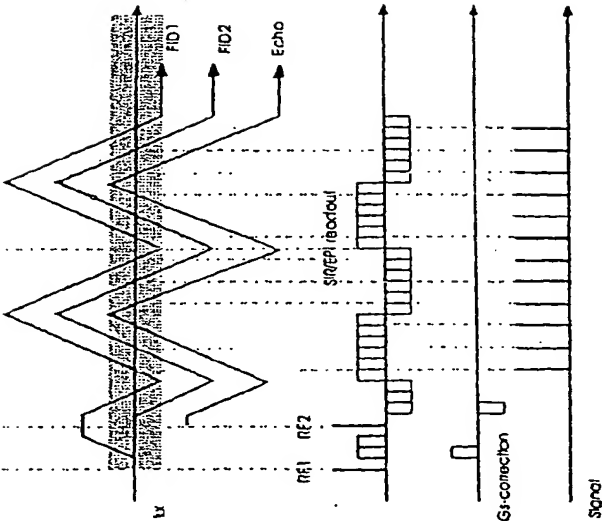


FIG. 12



FIG. 13
velocity encoding
pulses

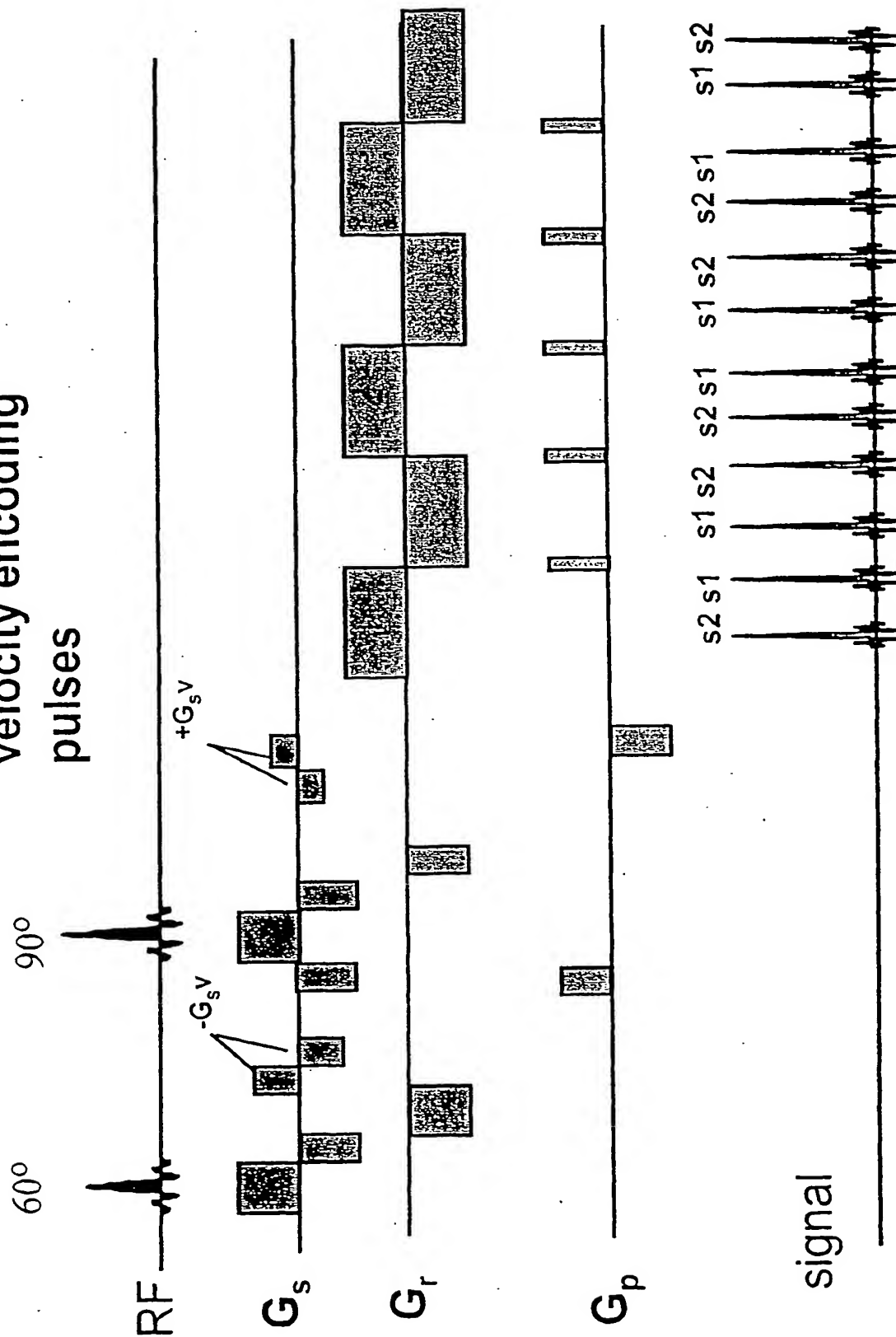
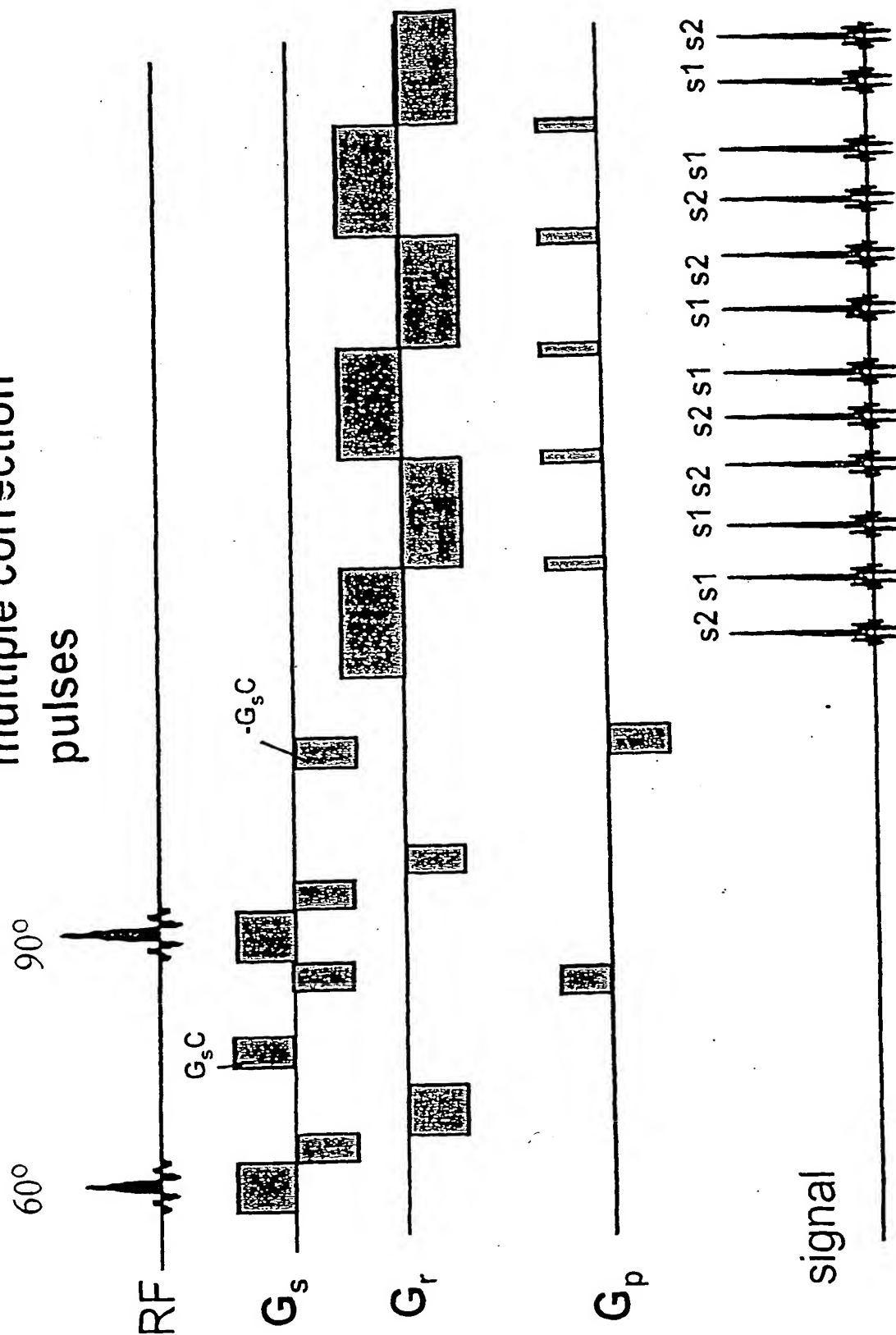


FIG. 14
multiple correction
pulses



**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☐ FADED TEXT OR DRAWING
- ☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☒ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☐ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.